Received: 6 September 2022 | Revised: 26 December 2022 | Accepted: 7 February 2023

DOI: 10.1111/sdi.13148

ORIGINAL ARTICLE

Seminars in Dialysis WILEY

Piperacillin-tazobactam dosing in anuric acute kidney injury patients receiving continuous renal replacement therapy

Dhakrit Rungkitwattanakul[1] | Taniya Charoensareerat[2] | Ekanong Chaichoke[2] | Thanakorn Rakamthong[2] | Pitchaya Srisang[2] | Sutthiporn Pattharachayakul[3] | Nattachai Srisawat[4] | Weerachai Chaijamorn[2]

[1]Department of Clinical and Administrative Pharmacy Sciences, College of Pharmacy, Howard University, Washington, District of Columbia, USA

[2]Faculty of Pharmacy, Siam University, Bangkok, Thailand

[3]Department of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Songkhla, Thailand

[4]Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Correspondence
Weerachai Chaijamorn, Faculty of Pharmacy Siam University, 38 Petchkasem Rd, Bang Wa, Phasi Charoen, Bangkok 10160, Thailand.
Email: weerachai.cha@siam.edu

Funding information
This study was supported by a grant from the Siam University. The funding source had no role in: the study design; the collection, analysis, and interpretation of data; and the writing of the article and the decision to submit it for publication.

Abstract

Introduction: To determine appropriate dosing of piperacillin-tazobactam in critically ill patients receiving continuous renal replacement therapy (CRRT).

Methods: The databases of PubMed, Embase, and ScienceDirect were searched. We used the Medical Subject Headings of "piperacillin-tazobactam," "CRRT," and "pharmacokinetics" or related terms or synonym to identify the studies for reviews. A one-compartment pharmacokinetic model was conducted to predict piperacillin levels for the initial 48 h of therapy. The pharmacodynamic target was 50% of free drug level above the minimum inhibitory concentration (MIC) and 4 times of the MIC. The dose that achieved at least 90% of the probability of target attainment was defined as an optimal dose.

Results: Our simulation study reveals that the dosing regimen of piperacillin-tazobactam 12 g/day is appropriate for treating Pseudomonal infection with KDIGO recommended effluent rate of 25–35 mL/kg/h. The MIC values of each setting were an important factor to design piperacillin-tazobactam dosing regimens.

Conclusion: The Monte Carlo simulation can be a useful tool to evaluate drug dosing in critically ill acute kidney injury patients receiving CRRT when limited pharmacokinetic data are a concern. Clinical validation of these results is needed.

1 | INTRODUCTION

Continuous renal replacement therapy (CRRT) is often required for critically ill patients with acute kidney injury (AKI).[1] AKI in the intensive care unit (ICU) is frequently associated with septic shock caused by severe infections.[2] It is established that timely administration of antimicrobial agents is crucial to survival rates of the patients. However, several factors in the ICU can affect serum drug concentration resulting suboptimal drug efficacy, namely, increased volume of distribution, protein binding alteration, and extracorporeal drug clearance.[3] Piperacillin-tazobactam is a beta-lactam antibiotic commonly used for empirical or documented therapy in critically ill patients. It is a combination of two agents consisting of an extended-spectrum beta-lactam antimicrobial (piperacillin) and a beta-lactamase inhibitor (tazobactam). Piperacillin possesses activity against a wide range of Gram-negative organisms, including *Escherichia coli*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* and is highly tolerated.[4] Tazobactam inhibits the activity against beta-lactamase enzymes but not directly to the organisms. In patients with intact renal function, piperacillin has a moderate protein binding (30%) and a relatively hydrophilic with the volume of distribution of 0.24 L/kg. Tazobactam has similar pharmacokinetic profile to piperacillin (low volume of distribution, 18.2-L moderate plasma protein binding, 30%, and clearance, 250 mL/min).[4,5] In critically ill patients, piperacillin clearance ranges from 3.12 to 19.9 L/h where tazobactam clearance ranges from 5.1 to 6.78 L/h.[4] Due to its properties, both piperacillin and tazobactam are subjected to be effectively cleared by CRRT treatments.[6]

